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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/03/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/870,012

Applicant(s)

KHOSLA ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period of Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-24 is/are pending in the application.
- 4a) Of the above claim(s) 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 5, mailed on July 22, 2002), Applicants filed an election and an amendment received on August 26, 2002 (Paper No. 7). Said amendment amended Claims 20-23 and added new Claim 24. Thus, Claims 18-24 are pending in the instant Office action.

Election

2. Applicant's election without traverse of Group II, Claim 19, in Paper No. 7 is acknowledged. Applicants' amendment of Claims 20-23 group said claims with the elected Group. Also, newly added Claim 24 is drawn to the elected Group. Thus, Claims 19-24 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/003,338 filed on July 6, 1995 and the U.S. non-Provisional Application No. 08/675,817 (now USPN 6,080,555) filed on July 5, 1996 as requested in the declaration and the first lines of the specification. Neither of these applications, however, disclosed the claimed invention of Claims 19-24.

The instant application is granted the benefit of priority for the U.S. non-Provisional Application No. 08/896,323 (USPN 6,066,721) filed on July 17, 1997 and the U.S. non-Provisional Application No. 08/434,289 (now USPN 6,261,816) filed on November 5, 1999 as

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requested in the first lines of the specification. These applications do disclose the claimed invention. Thus, the earliest effective filing date of the claimed invention is considered to be July 17, 1997.

Information Disclosure Statement

4. The information disclosure statements filed on March 5, 2002 (Paper No. 3) and August 26, 2002 (Paper No. 6) have been reviewed, and their references have been considered as shown by the Examiner's initials next to each citation on the attached copies.

Objections to the Specification

5. The specification is objected to for lacking updated continuity data in the first paragraph. The instant application claims the benefit of U.S. non-Provisional Application No. 09/424,289 filed on November 5, 1999; this citation must be updated to include the USPN 6,261,816. Appropriate amendment to the specification is required (see M.P.E.P. § 201.11).

6. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Methods of Prepare Antibiotics using Mutant Saccharopolyspora erythraea Host Cells
Supplied with Macrolides---

7. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in

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foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Abstract of the instant application is wholly inadequate to describe the disclosed subject matter. The Examiner suggests the inclusion of the following: the concept of disarming native ketosynthase (KS) starter units in polyketide synthase (PKS) gene clusters to facilitate the feeding of non-native starter units to produce novel polyketides, the use of *S. erythraea* and *S. coelicolor*, and the use of the erythromycin PKS gene cluster. The Abstract should be in the form of a single paragraph.

Claim Objections

8. Claim 24 is objected to for omitting where the structure of Formula 7 can be found in the specification. The Examiner suggests the inclusion of ---as depicted in Figure 3--- at the end of the claim to obviate this objection.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 19-24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms “macrolide” and “antibiotic” as used in the claims are unclear to the extent that they can mean the same thing. As found in Stedman’s Medical Dictionary, 27th Edition (on-line), the definition of “macrolide” includes “several antibiotics, including erythromycin”. Thus, antibiotic can be a subset of macrolides. When exactly does a

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macrolide become and antibiotic in its biosynthesis? As soon as it has any anti-bacterial activity? Most antibiotic precursors could fall into this broad definition. Thus, the metes and bounds of the terms are unclear. Appropriate clarification is required.

10. Claims 22 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviation “6-dEB” is used in the claims without definition upon its first occurrence. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 20 is rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 20 is drawn to methods of using *S. erythraea*, wherein said cells are described only by function, i.e., producing no macrolide.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject

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matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a single example of an *S. erythraea* cell that produces no macrolide is described in the form of the A34 mutant taught by Weber *et al.* No structural information about this mutant is described. While methods using this particular mutant strain are adequately described in the specification, the specification is wholly devoid and any structure of mutants to be used in the instant claim so that one of skill in the art would be able to predict the structure of other members of the genus of cell strains used in the claims. Thus, the instant claim is not described to the full extent of its scope in the specification as originally filed.

12. Claims 21-24 are rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the claimed invention, one of skill in the art is required to utilize an *Streptomyces erythraea* A34 mutant as described in Weber *et al.* (J. Bacteriol. (1985)

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164:425-433). The Examiner notes that *Streptomyces erythraea* is another name for *Saccharopolyspora erythraea* (see attachment).

To practice the instant methods, one of skill in the art is required to use the A34 mutant. It is not clear from Weber *et al.* how to make the A34 mutant using publicly available resources. Thus, its deposit is required. To enable the instant claims by enabling the deposit of A34, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and full address of the depository (37 C.F.R. § 1.801 - 1.809), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

13. Claims 19 and 20 are rejected under 35 U.S.C. § 102(e) as being anticipated by Katz *et al.* (USPN 5,824,513). The instant claims are drawn to methods of making antibiotics using a

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mutant *Saccharopolyspora erythraea* host cells that has been fed a macrolide that acts as a precursor in the biosynthetic pathway of the antibiotic.

Katz *et al.* teach "alterations which will result in the production of macrolide rings only when fed exogenously with substrate analogs, e.g. thioesters of appropriate acyl compounds of various lengths" (see column 4, lines 9-15). More specifically, in Examples 19-21, a mutant *S. erythraea* AKS1, whose KS1 allele has been mutated in its chromosome, is fed a butyl thioester of a δ -lactone to produce an antibiotic as tested by the antibiotic-sensitive microorganism, *S. aureus* (see columns 13-14).

Conclusion

14. No claims are allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229.

The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK

November 27, 2002

